

This Page Is Inserted by IFW Operations  
and is not a part of the Official Record

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning documents *will not* correct images,  
please do not report the images to the  
Image Problem Mailbox.**

**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>5</sup> :</b> C08F 30/08, 291/00, 22/10, C07C 7/08, G02B 1/04, C08F 290/06	<b>A1</b>	<b>(11) International Publication Number:</b> WO 94/21698 <b>(43) International Publication Date:</b> 29 September 1994 (29.09.94)
<b>(21) International Application Number:</b> PCT/US94/02379 <b>(22) International Filing Date:</b> 4 March 1994 (04.03.94) <b>(30) Priority Data:</b> 08/031,428 15 March 1993 (15.03.93) US <b>(71) Applicant:</b> BAUSCH & LOMB INCORPORATED [US/US]; One Chase Square, P.O. Box 54, Rochester, NY 14601-0054 (US). <b>(72) Inventors:</b> LAI, Yu-Chin; 23 Copper Woods, Pittsford, NY 14534 (US). BAMBURY, Ronald, E.; 63 Matthew Drive, Fairport, NY 14450 (US). <b>(74) Agents:</b> KRASNOW, David, M. et al.; Bausch & Lomb Incorporated, One Chase Square, P.O. Box 54, Rochester, NY 14601-0054 (US).		<b>(81) Designated States:</b> AU, BB, BG, BR, BY, CA, CN, CZ, FI, HU, JP, KP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
<b>(54) Title:</b> NOVEL FUMARATE AND FUMARAMIDE SILOXANE HYDROGEL COMPOSITIONS  <b>(57) Abstract</b>  Novel fumarate- and fumaramide-containing monomers are disclosed which are especially useful in the preparation of biocompatible devices, especially contact lenses.		

*FOR THE PURPOSES OF INFORMATION ONLY*

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	GB	United Kingdom	MR	Mauritania
AU	Australia	GE	Georgia	MW	Malawi
BB	Barbados	GN	Guinea	NE	Niger
BE	Belgium	GR	Greece	NL	Netherlands
BF	Burkina Faso	HU	Hungary	NO	Norway
BG	Bulgaria	IE	Ireland	NZ	New Zealand
BJ	Benin	IT	Italy	PL	Poland
BR	Brazil	JP	Japan	PT	Portugal
BY	Belarus	KE	Kenya	RO	Romania
CA	Canada	KG	Kyrgyzstan	RU	Russian Federation
CF	Central African Republic	KP	Democratic People's Republic of Korea	SD	Sudan
CG	Congo	KR	Republic of Korea	SE	Sweden
CH	Switzerland	KZ	Kazakhstan	SI	Slovenia
CI	Côte d'Ivoire	LI	Liechtenstein	SK	Slovakia
CM	Cameroon	LK	Sri Lanka	SN	Senegal
CN	China	LU	Luxembourg	TD	Chad
CS	Czechoslovakia	LV	Latvia	TG	Togo
CZ	Czech Republic	MC	Monaco	TJ	Tajikistan
DE	Germany	MD	Republic of Moldova	TT	Trinidad and Tobago
DK	Denmark	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	US	United States of America
FI	Finland	MN	Mongolia	UZ	Uzbekistan
FR	France			VN	Viet Nam
GA	Gabon				

## NOVEL FUMARATE AND FUMARAMIDE SILOXANE HYDROGEL COMPOSITIONS

### BACKGROUND OF THE INVENTION

#### Field of the Invention

The present invention relates to novel fumarate- and polyfumaramide-containing monomers and compositions comprising the monomers. Especially preferred are the polyfumarate- and polyfumaramide-containing compositions used to make highly oxygen permeable hydrogels which may be used to make biomedical devices including contact lenses.

#### Background

In the field of contact lenses, various factors must combine to yield a material that has appropriate characteristics. Polysiloxane materials are useful materials for making contact lenses due to, among other properties, their excellent oxygen permeability. See U.S. Patent Nos. 4,153,641 and 4,189,546. However, certain polysiloxane materials are known to experience poor wetting.

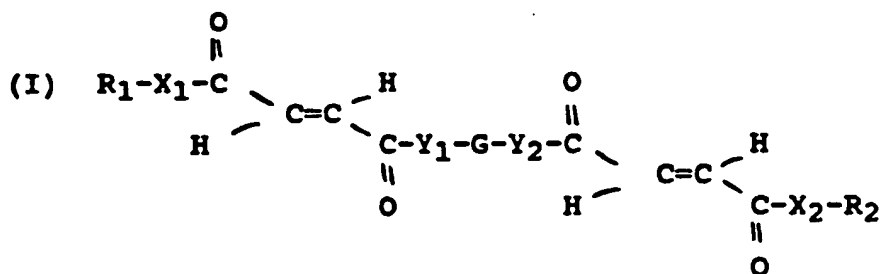
Difunctional groups such as fumarates and maleates are known to be viable wetting comonomers in certain polysiloxane copolymeric systems. However, it is well known by those

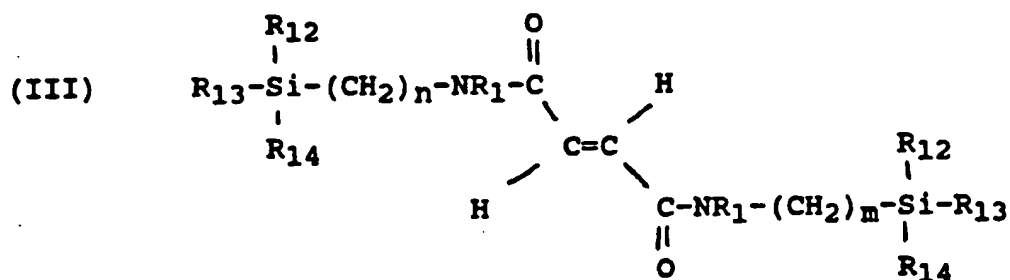
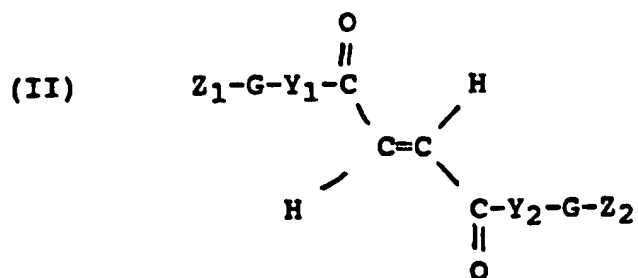
skilled in the field that fumarates often do not easily polymerize into high molecular weight polymers due to steric hindrance.

Certain bulky siloxane-containing fumarates, including bis(siloxanylalkyl)fumarate and (poly)alkylfluoroalkyl fumarates, reportedly may be used as copolymers to make hard contact lens materials. (See European Patent Application No. 86114829.4.) However, the known polymerization schemes for such fumarate-containing polymers, which are directed exclusively to hard contact lens materials, require a minimum of at least 24 hours of curing, and achieve only a low yield of the desired polymer.

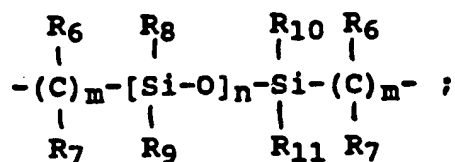
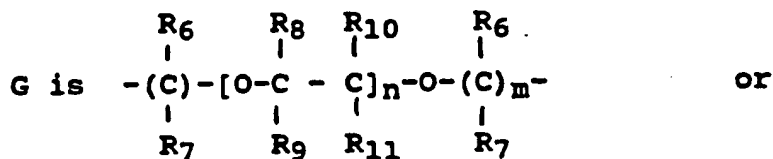
#### SUMMARY OF THE INVENTION

In accordance with the present invention novel wettable fumarate- and fumaramide-containing monomers are disclosed for use with both silicone and non-silicone containing polymeric systems used for biomedical devices, especially contact lenses. The novel monomers have the following schematic representations:





wherein



$\text{X}_1$ ,  $\text{X}_2$ ,  $\text{Y}_1$  and  $\text{Y}_2$  are independently O or  $\text{NR}_4$ , except that when G is siloxane-containing,  $\text{X}_1$  and  $\text{X}_2$  must be  $\text{NR}_4$ ;

$\text{Z}_1$  and  $\text{Z}_2$  are independently  $\text{OR}_3$  or  $\text{NR}_4\text{R}_5$ ;

R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> are independently H or an alkyl group having 1 to 10 carbon atoms;

R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub>, R<sub>9</sub>, R<sub>10</sub> and R<sub>11</sub> are independently hydrogen or an alkyl-containing or fluoroalkyl-containing group having 1 to 10 carbon atoms which may have ether linkages between two carbon atoms;

R<sub>12</sub>, R<sub>13</sub> and R<sub>14</sub> are independently methyl, trimethylsiloxy or pentylmethyldisiloxanyloxy;

m is 1 to 10; and

n is 5 to 100.

#### DETAILED DESCRIPTION OF THE INVENTION

The ease with which the fumarate- and fumaramide-containing monomers of this invention are polymerized into useful polymers was unexpected. The monomer mixes containing the fumarate- and fumaramide-containing monomers are able to be cured within approximately two to four hours which is significantly faster than any known fumarate-containing systems. The novel fumarate monomers of the present invention, therefore enable the attributes of fumarate chemistry to be used in new fields.

While the present invention contemplates the use of novel fumarate- and fumaramide-containing polymers for both "hard"

and "soft" contact lenses, the formulations containing the fumarate- and fumaramide-containing monomers of the present invention are thought to be especially useful as soft hydrogel contact lenses. As is understood in the field, a lens is considered to be "soft" if it can be folded back upon itself without breaking.

A hydrogel is a hydrated cross-linked polymeric system that contains water in an equilibrium state. Silicone hydrogels (i.e., hydrogels containing silicone) are usually prepared by polymerizing a mixture containing at least one silicone-containing monomer and at least one hydrophilic monomer. Either the silicone-containing monomer or the hydrophilic monomer may function as a crosslinking agent (a crosslinker), being defined as a monomer having multiple polymerizable functionalities. Additional crosslinkers also may be present in the monomer mix which polymerizes to form the hydrogel.

The fumarate- and fumaramide-containing monomers of the present invention have at least one fumarate or fumaramide group. Monomer mixes comprising the novel monomers of the present invention may comprise both thermal- and photoinitiators for curing purposes. The monomer mixes may further comprise at least one additional hydrophilic monomer. Further, the monomer mix may additionally comprise at least one siloxane-containing monomer.



In further embodiments of the present invention, the novel monomers are used to make biomedical devices and are useful in formulations for silicone-containing and non-silicone-containing contact lenses which may be either "soft" or "hard" and which may preferably be hydrogels.

As is known in the field, certain crosslinked polymeric materials may be polymerized to form a hard water-free xerogel. Xerogels are understood to be unhydrated hydrogel formulations. It was found that such xerogels could be physically altered to, for example, impart optical properties through machining, and then be hydrated and retain their water content.

When the term "polymerization" is used herein we refer to the polymerization of the double bonds of the monomers and prepolymers endcapped with polymerizable unsaturated groups which results in a crosslinked three dimensional network.

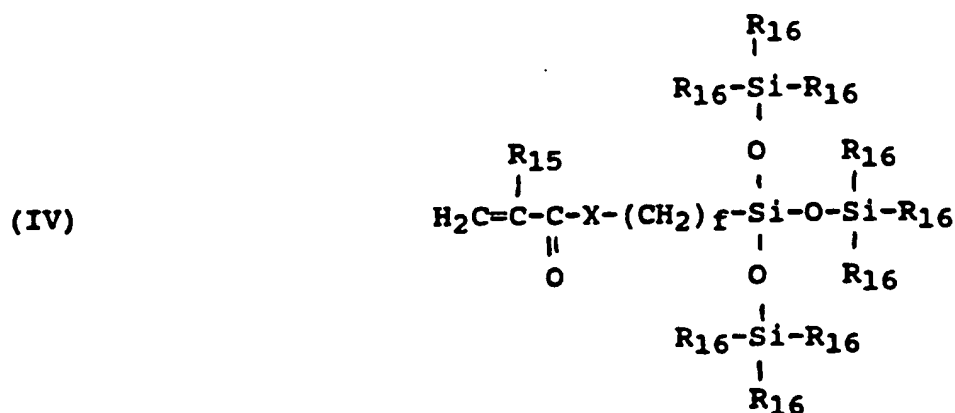
Further, notations such as "(meth)acrylate" or "(meth)acrylamide" are used herein to denote optional methyl substitution. Thus, for example, methyl (meth)acrylate includes both methyl acrylate and methyl methacrylate and N-alkyl(meth)acrylamide includes both N-alkyl acrylamide and N-alkyl methacrylamide.

The term "prepolymer" denotes a high molecular weight monomer containing polymerizable groups. The monomers added to the monomeric mixture of the present invention may therefore be monomers or prepolymers. Thus, it is understood that the term "silicone-containing monomers" includes "silicone-containing prepolymers".

The terms "shaped articles for use in biomedical applications" or "biomedical devices or materials" or "biocompatible materials" mean the hydrogel materials disclosed herein have physicochemical properties rendering them suitable for prolonged contact with living tissue, blood and the mucous membranes.

The fumarate- and fumaramide-containing monomers of the present invention may be prepared according to syntheses well-known in the art and according to the methods disclosed in the following examples.

As mentioned previously, additional silicone-containing monomers may be present in the monomer mixes with the fumarate or fumaramide-containing monomers. One preferred class of suitable silicone-containing monomers which may be incorporated into a monomer mix with the fumarate or fumaramide-containing monomers of the present invention are the bulky polysiloxanylalkyl (meth)acrylic monomers represented by the following formula (IV):



wherein:

X is O or NR;

each R<sub>15</sub> is independently hydrogen or an alkyl group having 1 to 10 carbon atoms; and

each R<sub>16</sub> is independently a lower alkyl or phenyl group;

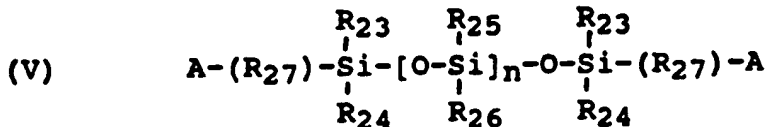
and

f is 1 or 3 to 10.

Such bulky monomers include methacryloxypropyl tris(trimethylsiloxy)silane, pentamethyldisiloxanylmethylmethacrylate, tris(trimethylsiloxy)methacryloxy propylsilane, phenyltetramethyldisiloxanylethyl acetate, and methyldi(trimethylsiloxy)methacryloxymethyl silane.

A further preferred class of silicone-containing monomers which may be incorporated into a monomer mix with the fumarate- or fumaramide-containing monomers of the present

invention are the poly(organosiloxane) monomers represented by the following formula (V):



wherein:

A is an activated unsaturated group, such as an ester or amide of an acrylic or a methacrylic acid;

each  $R_{23}$ - $R_{26}$  is independently selected from the group consisting of a monovalent hydrocarbon radical or a halogen substituted monovalent hydrocarbon radical having 1 to 18 carbon atoms which may have ether linkages between carbon atoms;

$R_{27}$  is a divalent hydrocarbon radical having from 1 to 22 carbon atoms;

and

n is 0 or an integer greater than or equal to 1.

Further, hydrophilic monomers may also be incorporated into the monomer mixes to form hydrogels. Such preferred hydrophilic monomers may be either acrylic- or vinyl-containing monomers. Such hydrophilic monomers may be used as crosslinking agents. The term "vinyl-type" or "vinyl-containing" monomers refers to non-acrylic monomers containing the vinyl grouping ( $CH_2=CH_2$ ). Such hydrophilic vinyl-containing monomers are known to polymerize relatively easily.

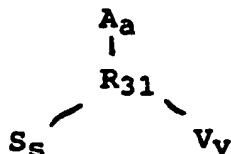
"Acrylic-type" or "acrylic-containing" monomers are those monomers containing the acrylic group ( $\text{CH}_2=\text{C}(\text{R})\text{X}$ ) wherein R = H or  $\text{CH}_3$  and X is O or NH.

When siloxane-containing monomers are incorporated into the monomer mix, the weight % of the siloxane-containing monomers as compared to the total monomer mix weight % is from about 5% to 80%, more preferably from about 20% to 75%, and most preferably 40% to 70%. The relative weight % of hydrophilic monomer(s) to total weight % of the comonomer mix is preferably from about 5% to 80%, more preferably from about 20% to 70%, and most preferably 30% to 60%.

Preferred hydrophilic vinyl-containing monomers which may be incorporated into the hydrogels of the present invention include monomers such as N-vinyl lactams (e.g. N-vinyl pyrrolidone (NVP)), N-vinyl-N-methyl acetamide, N-vinyl-N-ethyl acetamide, N-vinyl-N-ethyl formamide, N-vinyl formamide, with NVP being the most preferred.

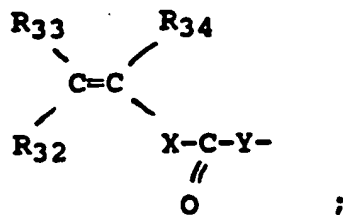
Preferred hydrophilic acrylic-containing monomers which may be incorporated into the hydrogel of the present invention include hydrophilic monomers such as N,N-dimethyl acrylamide (DMA), 2-hydroxyethyl methacrylate, glycerol methacrylate, 2-hydroxyethyl methacrylamide, methacrylic acid and acrylic acid, with DMA being the most preferred.

When it is desirable for both an acrylic-containing wetting monomer and a vinyl-containing wetting monomer to be incorporated into the silicone-containing polymer of the present invention, a further crosslinking agent having both a vinyl and an acrylic polymerizable group may be used, since these vinyl and acrylic wetting monomers have greatly differing reactivity ratios and do not copolymerize efficiently. Such crosslinkers which facilitate the copolymerization of these monomers are the subject of presently co-pending and commonly assigned U.S. Patent Application No. 07/922,452 filed July 30, 1992. Such crosslinkers are represented by the following schematic representation:

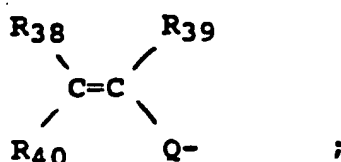


wherein

V denotes a vinyl-containing group having the formula:



S denotes a styrene-containing group having the formula:



wherein

R<sub>31</sub> is an alkyl radical derived from substituted and unsubstituted hydrocarbons, polyalkylene oxide, poly(perfluoro) alkylene oxide, dialkyl-capped polydimethylsiloxane, dialkyl-capped polydimethylsiloxane modified with fluoroalkyl or fluoroether groups;

R<sub>32</sub>-R<sub>40</sub> are independently H, or alkyl of 1 to 5 carbon atoms;

Q is an organic group containing aromatic moieties having 6-30 carbon atoms;

X, Y, and Z are independently O, NH or S;

v is 1, or higher; and

a, s are independently greater than or equal to 0; and

a + s is greater than or equal to 1.

Such crosslinkers help to render the monomer mix totally UV-curable. It was further discovered that the use of UV initiators in the monomer mix allowed the fumarate- and fumaramide-containing monomer mixes to cure at surprisingly and unexpectedly rapid rates. This enhanced curing rate is thought to apply to fumarate- and fumaramide-containing monomers which are beyond the scope of the present application. The enhanced curing of fumarates and fumaramides is the subject of a concurrently filed and commonly assigned U.S. Patent Application (which has not yet received a U.S. Serial No., but which corresponds to Attorney Docket) No. P01050.

Other crosslinking agents which may be incorporated into the silicone-containing hydrogel of the present invention include polyvinyl, typically di- or tri-vinyl monomers, most commonly the di- or tri(meth)acrylates of dihydric ethylene glycol, triethylene glycol, butylene glycol, hexane-1,6-diol, thio-diethylene glycol-diacrylate and methacrylate; neopentyl glycol diacrylate; trimethylolpropane triacrylate and the like; N,N'-dihydroxyethylene-bisacrylamide and - bismethacrylamides; also diallyl compounds like diallyl phthalate and triallyl cyanurate; divinylbenzene; ethylene glycol divinyl ether; and the (meth)acrylate esters of polyols such as triethanolamine, glycerol, pentanerythritol, butylene glycol, mannitol, and sorbitol. Further, illustrations include N,N-methylene-bis-(meth)acrylamide, sulfonated



divinylbenzene, and divinylsulfone. Also useful are the reaction products of hydroxyalkyl (meth)acrylates with unsaturated isocyanates, for example the reaction product of 2-hydroxyethyl methacrylate with 2-isocyanatoethyl methacrylate (IEM). See U.S. Patent No. 4,954,587.

Other known crosslinking agents are polyether-bisurethane-dimethacrylates (see U.S. Patent No. 4,192,827), and those crosslinkers obtained by reaction of polyethylene glycol, polypropylene glycol and polytetramethylene glycol with 2-isocyanatoethyl methacrylate (IEM) or m-isopropenyl-~~8,8~~, -dimethylbenzyl isocyanates (m-TMI), and polysiloxane-bisurethane-dimethacrylates. See U.S. Patent Nos. 4,486,577 and 4,605,712. Still other known crosslinking agents are the reaction products of polyvinyl alcohol, ethoxylated polyvinyl alcohol or of polyvinyl alcohol-co-ethylene with 0.1 to 10 mol % vinyl isocyanates like IEM or m-TMI.

The monomers of the present invention, when copolymerized, are readily cured to cast shapes by methods such as UV polymerization, use of free radical thermal initiators and heat, or combinations thereof. Representative free radical thermal polymerization initiators are organic peroxides, such as for example acetal peroxide, lauroyl peroxide, decanoyl peroxide, stearoyl peroxide, benzoyl peroxide. tertiary butyl peroxyphthalate, peroxydicarbonate, and the commercially available thermal initiators such as

Lupersol 256, 225 and the like, employed in a concentration of about 0.01 to 2 percent by weight of the total monomer mixture. Representative UV initiators are those known in the field such as, benzoin methyl ether, benzoin ethyl ether, Darocur-1173, 1164, 2273, 1116, 2959, 3331 (EM Industries) and Igracure 651 and 184 (Ciba-Geigy).

In addition to the above-mentioned polymerization initiators, the copolymer of the present invention may also include other monomers as will be apparent to one skilled in the art. For example, the monomer mix may include additional colorants, or UV-absorbing agents and toughening agents such as those known in the contact lens art.

The resulting copolymers of this invention can be formed into contact lenses by the spincasting processes such as those disclosed in U.S. Pat. Nos. 3,408,429 and 3,496,254 and other conventional methods, such as compression molding as disclosed in U.S. Pat. Nos. 4,084,459 and 4,197,266.

Polymerization of the monomer mix may be conducted either in a spinning mold, or a stationary mold corresponding to a desired contact lens shape. The thus-obtained contact lens may be further subjected to a mechanical finishing, as occasion demands. Also, the polymerization may be conducted in an appropriate mold or vessel to give a lens material in the form of button, plate or rod, which may then be processed

(e.g., cut or polished via lathe or laser) to give a contact lens having a desired shape.

The hydrogels produced by the present invention are oxygen transporting, hydrolytically stable, biologically inert, and transparent. The monomers and prepolymers employed in accordance with this invention, are readily polymerized to form three dimensional networks which permit the transport of oxygen and are optically clear, strong and hydrophilic.

The present invention provides materials which can be usefully employed for the fabrication of prostheses such as heart valves and intraocular lenses, as optical contact lenses or as films. More particularly, the present invention concerns contact lenses.

The present invention further provides articles of manufacture which can be used for biomedical devices, such as, surgical devices, heart valves, vessel substitutes, intrauterine devices, membranes and other films, diaphragms, surgical implants, blood vessels, artificial ureters, artificial breast tissue and membranes intended to come into contact with body fluid outside of the body, e.g., membranes for kidney dialysis and heart/lung machines and the like, catheters, mouth guards, denture liners, intraocular devices, and especially contact lenses.

It is known that blood, for example, is readily and rapidly damaged when it comes into contact with artificial surfaces. The design of a synthetic surface which is antithrombogenic and nonhemolytic to blood is necessary for prostheses and devices used with blood.

The following examples serve only to further illustrate aspects of the present invention and should not be construed as limiting the invention.

#### EXAMPLE 1

##### Preparation of bis-3-(trimethylsiloxy)silyl propyl fumaramide.

Dry, basic alumina (11.48 g), 3-aminopropyl tris(trimethylsiloxy)silane (7.375 g, 0.02 mol) and 30 mL of methylene chloride were added into a dry 250 mL round bottom flask equipped with a mechanical stirrer and nitrogen blanket. The mixture was cooled with an ice bath at 0-5 degrees C. Fumaryl chloride (1.527 g, 0.01 mol) was then added over a period of two hours while the mixture was kept cold. The solution was then extracted twice with 2 N HCl, then twice with 60 mL 0.5 N NaOH, followed by 60 mL water (three times). The solution was then concentrated and eluted through silica gel column with a 20:80 methylene chloride:methanol solution. The purified named product was recovered by evaporating the solvent yielding 0.8 g. The purified product melted at 172-

174 degrees C.  $^1\text{H}$ -NMR gave the following peaks: 0.05 ppm (singlet, 4H); 2.30 ppm (multiplet, 4H); 1.40 ppm (multiplet, 4H); 3.12 ppm (multiplet, 4H); 6.72 ppm (singlet, 2H); and 6.90 ppm (singlet, 2H). IR gave the peaks characteristic of the structure ( $-\text{CH}_3$ ),  $1630\text{cm}^{-1}$  (amide I),  $1550\text{cm}^{-1}$  (amide II).

## EXAMPLE 2

### Preparation of bis(4-hydroxybutyl) tetramethyl disiloxane-based fumarate monomer end-capped with t-butylamine.

Into a 2-neck, 500 mL round bottom flask connected to a nitrogen blanket and reflux condenser was added 6.95 g (0.027 mol.), bis(4-hydroxybutyl) tetramethyldisiloxane, 8.274 g (0.054 mol) of fumaryl chloride and 200mL of dry toluene. The mixture was brought to 90 degrees C and stirred. After 4 hours, the reaction was found to be complete by checking an aliquot with infrared spectroscopy. The mixture was vacuum stripped to remove excess fumaryl chloride and toluene at 80 degrees C. The reaction mixture was then cooled and 250 mL of toluene was added. T-butyl amine (9.79 g) was added dropwise while the mixture was cooled to between 0 to 5 degrees C. After the addition of t-butylamine, the temperature was allowed to rise to room temperature. The product mixture was extracted with 0.1 N sodium bicarbonate aqueous solution and dried over magnesium sulfate. The liquid product was recovered after vacuum stripping of the solvent. The product crystallized after standing overnight to yield 12.8 g, or 81%.

## EXAMPLES 3-4

Preparation of polysiloxanediol-based fumarate prepolymers end-capped with t-butylamine

The preparations were conducted as described in Example 2 above except that polysiloxanediols of Mn (molecular weight average) 734 and Mn 1300 were used to prepare monomers designated as "F<sub>2</sub>D<sub>6</sub>" (Example 3) and "F<sub>2</sub>D<sub>15</sub>" (Example 4) respectively, instead of bis(4-hydroxybutyl) tetramethyl disiloxane. The designation "Mn" represents the molecular weight average of the polymeric structure. The purified products were clear fluids. IR spectrum (Examples 3 and 4) 3307cm<sup>-1</sup>, 2982cm<sup>-1</sup>, 1729cm<sup>-1</sup>, 1680cm<sup>-1</sup>, 1643cm<sup>-1</sup>, 1540cm<sup>-1</sup>, 1257cm<sup>-1</sup>, 1008cm<sup>-1</sup>, 786cm<sup>-1</sup>. H<sup>1</sup>-NMR spectrum (Example 4) 0.08ppm (Si-CH<sub>3</sub>); 0.58ppm (CH<sub>2</sub>-Si); 1.38ppm (-CH<sub>2</sub>-); 1.41ppm (t-butyl); 1.58ppm (NH); 1.70ppm (-CH<sub>2</sub>-); 4.19ppm (-CH<sub>2</sub>-); 6.73ppm (vinyl H).

## EXAMPLE 5

Alternate procedure for preparing polysiloxanediol-based fumarate prepolymers end-capped with t-butylamine.

The preparation was conducted in dry tetrahydrofuran (THF) at room temperature for step 1 and in dry THF at 0-5 degrees C at step 2. All other reaction and purification conditions were the same as those described in Example 2.

## EXAMPLE 6

Preparation of polysiloxanediol-based fumarate prepolymers end-capped with 3-aminopropyl pyrrolidone.

The preparation was conducted as described in Example 5, using a polysiloxanediol of Mn 1300, and a stoichiometric amount of 3-aminopropyl pyrrolidone in place of the t-butylamine.

## EXAMPLE 7

Preparation of polysiloxanediol-based fumarate prepolymer end-capped with 2-hydroxyethyl pyrrolidone.

The preparation of the named product was carried out by the method of Example 6 except that the 3-aminopropyl pyrrolidone was replaced with 2-hydroxyethyl pyrrolidone.

## EXAMPLE 8

Preparation of polypropylene glycol-based fumarate prepolymer end-capped with t-butylamine (F<sub>2</sub>PPG)

A fumarate-containing prepolymer based on polypropylene glycol of Mn 4,000 (PPG-4000) was prepared according to the procedure as described in Example 5 except that the polysiloxanediol was replaced with PPG-4000 in the same stoichiometric amount.

## EXAMPLE 9

Preparation of perfluoro polyethylene glycol-based fumarate prepolymer end-capped with t-butylamine.

A fumarate-containing prepolymer based on perfluoro polyethylene glycol (Mn 2000) is prepared according to the method as described in Example 5 except that the polysiloxanediol is replaced by the perfluoro ethylene glycol of the same stoichiometric amount.

## EXAMPLE 10

Preparation of bis(hydroxyalkyl)polysiloxanylalkyl fumarate (D<sub>12</sub>)<sub>2</sub>F.

Into a 2-neck, 500 ml round bottom flask connected to a reflux condenser, a dropping funnel and nitrogen blanket, was added 30.0 g (0.025 mol) of bis(4-hydroxybutyl)polysiloxane (Mn 1,200). Through the dropping funnel, 1.74 g (0.0125 mol) of fumaryl chloride in 20mL of dry toluene was added into the flask over a period of half an hour while the contents in the flask were heated to 80 degrees C and magnetically stirred. The heating was continued for 4 hours. An aliquot was checked with infrared spectroscopy and found to be free of acid chloride. The reaction was stopped and the product was extracted twice with 0.1 N sodium bicarbonate and twice with distilled water followed by drying over magnesium sulfate. The final clear fluid product was recovered by removing the toluene under vacuum at 80 degrees C. Yield 26.5 g.



## EXAMPLE 11

Film casting of a fumarate prepolymer

The fumarate prepolymer shown in Example 4 (F<sub>2</sub>D<sub>15</sub> end-capped with t-butylamine) was mixed with 1% Lupersol-256, a thermal initiator (\*\*\*Chemical Name and Source\*\*\*), and cured between two silane-treated glass plates at 80 degrees C for 20 hours. The released films were extracted with ethanol for 16 hours and then dried in vacuo at 80 degrees C for 16 hours.

## EXAMPLE 12

Film casting of fumarate prepolymer with a hydrophilic monomer and hydrophobic monomer into hydrogel films

A formulation containing the following was prepared: fumarate prepolymer of Example 2, 70 parts; N,N-dimethylacrylamide (DMA), 30 parts; 1 part Lupersol-256. The resulting clear mix was cured into films between two silane-treated glass plates at 80 degrees C for 20 hours. The released films were then extracted with ethanol for 16 hours, then dried in vacuo at 80 degrees C for 16 hours, followed by boiling water extraction for 4 hours and placed in phosphate buffered saline at pH 7.2.

## EXAMPLES 13-19

Film casting of fumarate prepolymer (t-butylamine capped) with hydrophilic monomer and 3-methacryloxypropyl tris(trimethylsiloxyl) silane (TRIS).

The following monomer mixes were prepared and cured and processed into hydrogel films according to the procedures of Example 12. Properties of the resultant films are shown below.

(Wt %)	Examples						
	13	14	15	16	17	18	19
Fumarate Formulation	F <sub>2</sub> D <sub>6</sub>	F <sub>2</sub> D <sub>6</sub>	F <sub>2</sub> D <sub>15</sub>	F <sub>2</sub> D <sub>15</sub>	F <sub>2</sub> D <sub>15</sub>	F <sub>2</sub> PPG	F <sub>2</sub> D <sub>15</sub>
Fumarate	70	35	70	35	33	35	25
TRIS	0	35	0	35	33	35	35
DMA	30	30	30	30	34	30	30
(D <sub>12</sub> ) <sub>2</sub> F	0	0	0	0	0	0	10

## EXAMPLE 20

Film Properties

The fumarate-containing films cast from the formulations of Examples 11-19 were characterized for key properties. The water contents and ethanol extractables for each formulation were determined gravimetrically. The tensile and tear properties were determined in buffered saline, according to the standard ASTM procedures 1708 and 1938 respectively. The oxygen permeabilities were determined by polarographic method with the consideration of edge effect. (See Fatt, Rasson and Melpolder, International Contact Lens Clinic, 14, 389, 1987).

## EXAMPLE 21

Contact angle/ wettability measurements

The contact angles of the surface of the fumarate films were measured by the captive bubble technique. The films were submerged in buffered saline solution and a bubble of air was attached to the undersurface of the film. The angle created by the intersection of the films and bubble surfaces was measured using a goniometer. The contact angles from cast lenses were also measured similarly. A lower contact angle represents a greater degree of hydrophilicity or surface film wettability.

Properties	Example No.								
	11	12	13	14	15	16	17	18	19
% extract	-	-	-	-	-	3.9	4.0	2.9	4.1
%water	0	15	19	18	30	21.9	24.7	26.8	20
O <sub>2</sub> Perm.Dk	318	7.5	100	90	181	138	116	46	137
Cont. angle	62	35	30	30	35	-	33	31	31
Modulus (g/mm <sup>2</sup> )	571	340	960	390	-	135	128	-	120
% elong.	11	35	12	28	-	100	103	-	99
Tear (g/mm)	--	31	2.7	4.6	-	7.0	6.0	-	5.5

## EXAMPLE 22

Hydrolytic stability testing of fumarate hydrogel films

The cured fumarate hydrogel films, after being extracted with solvent and dried in vacuo, were cut into disks weighing 30mg each, with a thickness of 250 microns. The disks were weighed while dry and then were submerged into buffered saline at pH 7.4 in 12 vials and sealed. After equilibration, the

films were placed in an oven at 80 degrees C. Three vials were taken out after 3, 5, 7 and 14 days and the dry weight and water contents were determined gravimetrically. The hydrolytic stabilities were reported as % weight loss over 14 days. Experimentally, it was determined that resultant hydrogels with a weight loss of 7% or less would be considered stable.

The water weight loss and the hydrogel films presented in Example 21 was less than 1.7% in 14 days, indicating the hydrogel films are hydrolytically stable. Separately, the hydrogel films were also subjected to 10 cycles of autoclave cycling at 121 degrees C. Each cycle lasted 30 minutes. There was no change in film appearance.

#### EXAMPLE 23-26

##### UV curing of fumarate films

The same fumarate formulations as those in Examples 16-19 were used, except that the thermal initiator was replaced by 1) 0.5 part benzoin methyl ether (BME) (Example 23); 2) 0.2 part BME and 0.5 part Lupersol-225 (Example 24); 3) 0.2 part Darocur-1173 (EM Industries) plus 0.5 part Lupersol-225 (Example 25) and 4) 0.2 part Darocur (Example 26). These formulations were cured between two glass plates and under UV for 2 hours. After curing, the films were processed by the

procedures as described in Example 12. The amounts of extractables and water content (%) were as follows:

	Example No.			
	23	24	25	26
Initiator	0.5 BME	0.2 BME	0.2 Darocur	0.2 Darocur
Extract. %	11.5	6.8	4.6	6.2
% Water	16.5	20.5	22.2	22.0

The cured films of the formulation in Example 21 had the following physical properties:

O <sub>2</sub> Permeability	126
Modulus, Dk(G/mm <sup>2</sup> )	125
%Elongation	95
Tear strength(g/mm)	8.5

#### EXAMPLE 27

##### Film casting of t-butylamine-capped F<sub>2</sub>D<sub>15</sub> formulation with higher DMA content

A monomer mix containing F<sub>2</sub>D<sub>15</sub>, 30 parts; TRIS, 30 parts; DMA 40 parts, and Darocur-1173, 0.2 part was cured under UV for 2 hours and then processed into hydrogel films as described in Example 13. The hydrogel films have the following properties:

%Extractables	8.0	Modulus (g/mm <sup>2</sup> )	87
%water content	36	%Elongation	140
O <sub>2</sub> permeability(Dk)	77	Tear strength(g/mm)	5.1

## EXAMPLES 28-31

Properties of fumarate hydrogels with N-vinyl pyrrolidone as hydrophilic monomer

The following formulations were prepared and cured under UV and then processed into hydrogel films as described in Example 13, with the corresponding hydrogel properties listed below:

	Example No.			
	28	29	30	31
Composition				
F <sub>2</sub> D <sub>15</sub>	35	30	20	20
TRIS	35	30	30	30
NVP	30	40	20	20
DMA	-	-	30	30
Hexanol	-	-	20	20
Darocur-1173	0.2	0.2	0.2	0.2
Lupersol-225	0.5	0.5	-	-

Physical Properties	Example No.			
	28	29	30	31
%Extract	5.9	11.4	4.4	1.0
%Water	17	33	41	41
O <sub>2</sub> Perm, Dk	157	113	57	58
Modulus (g/mm <sup>2</sup> )	810	621	193	168
Tear Strength	7.9	6.0	4.2	3.3

## EXAMPLES 32-34

Properties of hydrogel films derived from 3-aminopropylpyrrolidone-capped fumarate prepolymer F<sub>2</sub>D<sub>15</sub> and hydrophilic monomers

The monomer prepared in Example 6 was used in formulation studies and films were cast as described in Example 28-31, to give hydrogel films with the following properties:

	Example No.		
	32	33	34
Formulation(parts)			
F <sub>2</sub> D <sub>15</sub>	35	30	30
TRIS	35	40	30
DMA	30	30	40
Hexanol	20	20	20
Darocur-1173	0.2	0.2	0.2

## Physical Properties

	Example No.		
	32	33	34
Properties			
%Extractables	2.8	2.8	3.7
%Water	23.5	24.0	36.2
O <sub>2</sub> Permeability (Dk)	140	135	79
Modulus (g/mm <sup>2</sup> )	97	102	76
%Elongation	100	150	75
Tear Strength g/mm	6.9	10.4	5.0

## EXAMPLE 35

Cast Molding of F<sub>2</sub>D<sub>15</sub> (T-butylamine-capped)-containing monomer mix into hydrogel lenses

The following monomer mix was prepared: fumarate monomer end-capped with t-butylamine, (F<sub>2</sub>D<sub>15</sub>, Example 4), 30 parts; TRIS, 30 parts; DMA 40 parts; hexanol, 20 parts; Darocur-1173, 0.2 part. The mix was filtered through a 5-micron filter into a clean vial. Through an applicator, 60-90 microliters of the mix was injected, under an inert nitrogen atmosphere onto a clean plastic mold half and then covered with a second plastic mold half. The molds were then compressed and cured for 90 minutes in the presence of UV light (4200 microwatts). The molds were then opened mechanically and put into a beaker containing aqueous ethanol. The lenses were released from the

molds within from 10 minutes to 1 hour. The lenses were then extracted with ethanol for 48 hours, boiled in distilled water for 4 hours and inspected for cosmetic quality and dimension. Lenses passing inspection were thermally disinfected in phosphate buffered saline solution prior to on-eye evaluation.

#### EXAMPLE 36

##### Cast Molding of 3-aminopropyl pyrrolidone-capped F<sub>2</sub>D<sub>15</sub>-derived monomer mix into hydrogel lenses

The monomer mix of Example 34 was cast-molded and processes into lenses by following the same procedure as described in Example 35.

#### EXAMPLE 37

##### Clinical Evaluations

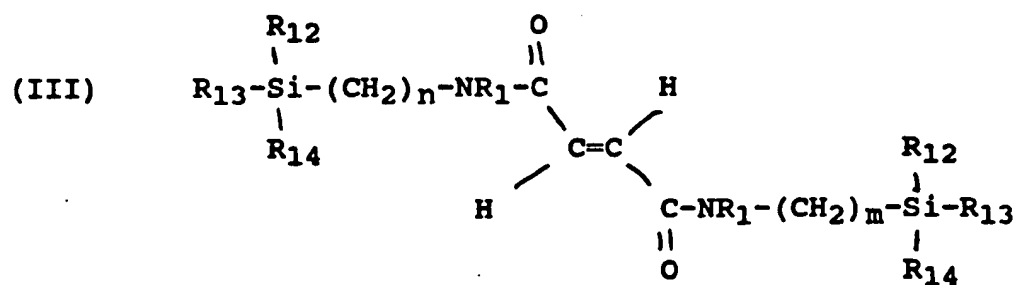
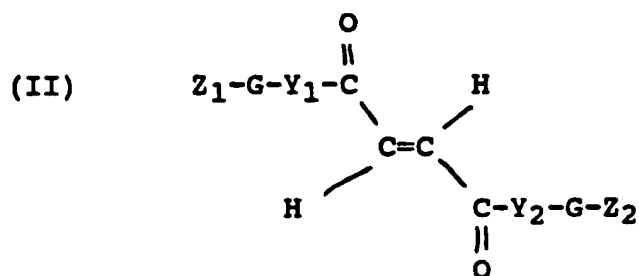
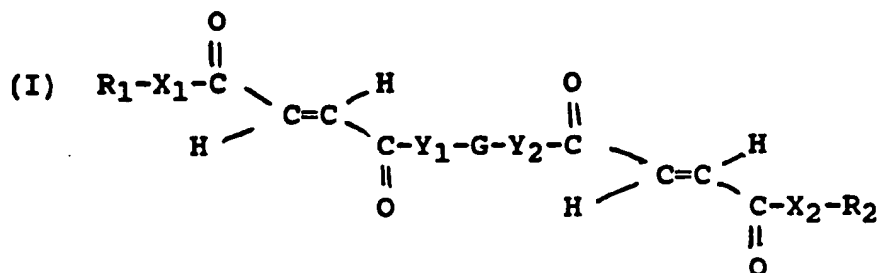
The cast molded polyfumarate hydrogel lenses described in Example 40 were evaluated on six to ten subjects. In each test, a poly(2-hydroxyethyl methacrylate) control lens was worn on one eye and the test lens on the other eye. The lenses were analyzed for wettability and surface deposition after a minimum of 4 hours wear. The polyfumarate lenses displayed excellent wetting equivalent to the poly(HEMA) control lenses. The polyfumarate lenses did display more deposits than their poly(HEMA) control counterparts, but were determined to be within an acceptable level.



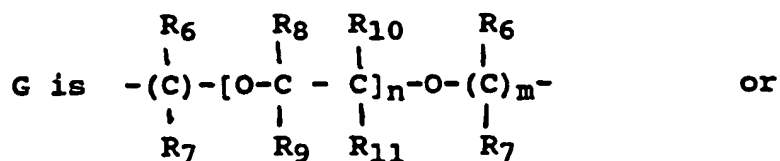
Many other modifications and variations of the present invention are possible and will be apparent to the skilled practitioner in the field in light of the teachings herein. It is therefore understood that, within the scope of the claims, the present invention can be practiced other than as herein specifically described.

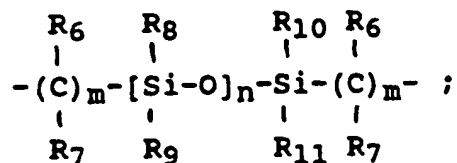
We Claim:

1. Fumarate-containing and fumaramide-containing monomers represented by the schematic representations:



wherein





$X_1$ ,  $X_2$ ,  $Y_1$  and  $Y_2$  are independently O or  $NR_4$ , except that when G is siloxane-containing,  $X_1$  and  $X_2$  must be  $NR_4$ ;

$Z_1$  and  $Z_2$  are independently  $OR_3$  or  $NR_4R_5$ ;

$R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$  and  $R_5$  are independently H or an alkyl group having 1 to 10 carbon atoms;

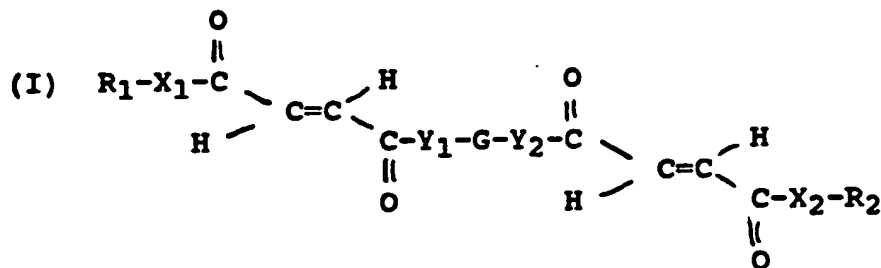
R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub>, R<sub>9</sub>, R<sub>10</sub> and R<sub>11</sub> are independently an alkyl-containing group having 1 to 10 carbon atoms, or fluoroalkyl-containing group having 1 to 10 carbon atoms;

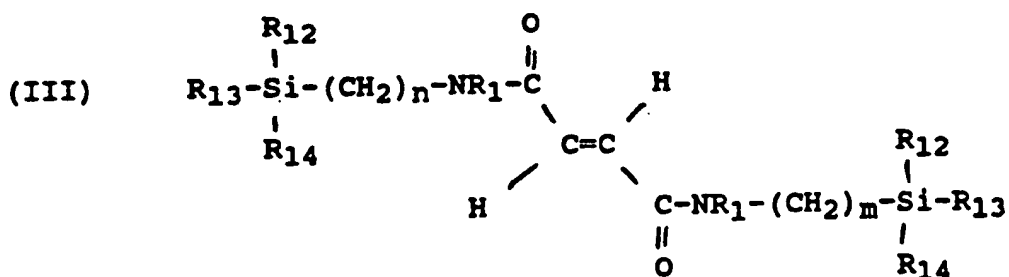
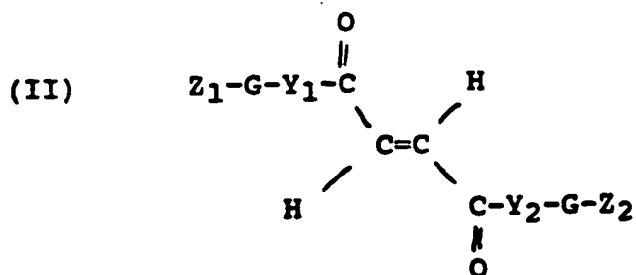
$R_{12}$ ,  $R_{13}$  and  $R_{14}$  are independently methyl, trimethylsiloxy or pentylmethyldisiloxanyloxy;

m is 1 to 10; and

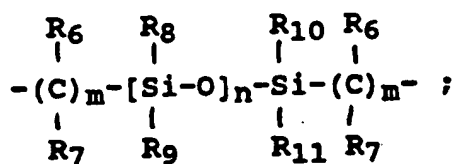
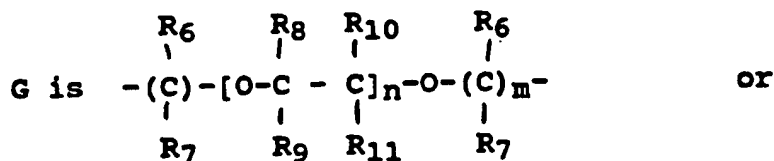
**n is 5 to 100.**

2. A monomer mix comprising a) at least one fumarate-containing or fumaramide-containing monomer having the following schematic representations:





wherein



$\text{X}_1$ ,  $\text{X}_2$ ,  $\text{Y}_1$  and  $\text{Y}_2$  are independently O or  $\text{NR}_4$ , except that when G is siloxane-containing,  $\text{X}_1$  and  $\text{X}_2$  must be  $\text{NR}_4$ ;

$\text{Z}_1$  and  $\text{Z}_2$  are independently  $\text{OR}_3$  or  $\text{NR}_4\text{R}_5$ ;

$\text{R}_1$ ,  $\text{R}_2$ ,  $\text{R}_3$ ,  $\text{R}_4$  and  $\text{R}_5$  are independently H or an alkyl group having 1 to 10 C atoms;

R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub>, R<sub>9</sub>, R<sub>10</sub> and R<sub>11</sub> are independently an alkyl-containing group having 1 to 10 C atoms, or fluoroalkyl-containing group having 1 to 10 C atoms;

R<sub>12</sub>, R<sub>13</sub> and R<sub>14</sub> are independently methyl, trimethylsiloxy or pentylmethyldisiloxanyloxy;

m is 1 to 10;

n is 5 to 100;

b) at least one hydrophilic monomer; and

c) at least one initiator.

3. The monomer mix of Claim 2 wherein said hydrophilic monomer is selected from the group consisting of N-vinyl pyrrolidone, N-vinyl-N-methyl acetamide, N-vinyl-N-ethyl acetamide, N-vinyl-N-ethyl formamide, N-vinyl formamide, N,N-dimethyl acrylamide, 2-hydroxyethyl methacrylate, glycerol methacrylate, 2-hydroxyethyl methacrylamide, methacrylic acid and acrylic acid.

4. The monomer mix of Claim 2 wherein said hydrophilic monomer is N,N-dimethylacrylamide.

5. The monomer mix of Claim 2 wherein said hydrophilic monomer is N-vinyl pyrrolidone.

6. The monomer mix of Claim 2 wherein said mix further comprises a hydrophobic monomer.

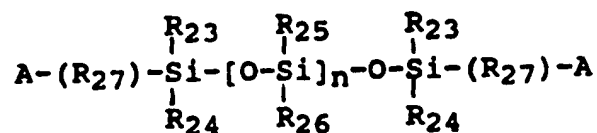
7. The monomer mix of Claim 2 wherein said mix further comprises a bulky polysiloxanylalkyl monomer.

8. The monomer mix of Claim 7 wherein said bulky polysiloxanylalkyl monomer is selected from the group consisting of methacryloxypropyl tris(trimethylsiloxy)silane, pentamethyldisiloxanylmethylmethacrylate, tris(trimethylsiloxy)methacryloxy propylsilane, phenyltetramethyldisiloxanylethyl acetate, and methyldi(trimethylsiloxy)methacryloxymethyl silane.

9. The monomer mix of Claim 7 wherein said bulky polysiloxanylalkyl monomer is methacryloxypropyl tris(trimethylsiloxy)silane.

10. The monomer mix of Claim 2 wherein said mix further comprises a polyorganosiloxane-containing monomer.

11. The monomer mix of Claim 10 wherein said polyorganosiloxane-containing monomer is a monomer represented by the formula:



wherein:

A is an activated unsaturated group, such as an ester or amide of an acrylic or a methacrylic acid;

each R<sub>23</sub>-R<sub>26</sub> is independently selected from the group consisting of a monovalent hydrocarbon radical or a halogen substituted monovalent hydrocarbon radical having 1 to 18 carbon atoms which may have ether linkages between carbon atoms;

R<sub>27</sub> is a divalent hydrocarbon radical having from 1 to 22 carbon atoms;

and

n is 0 or an integer greater than or equal to 1.

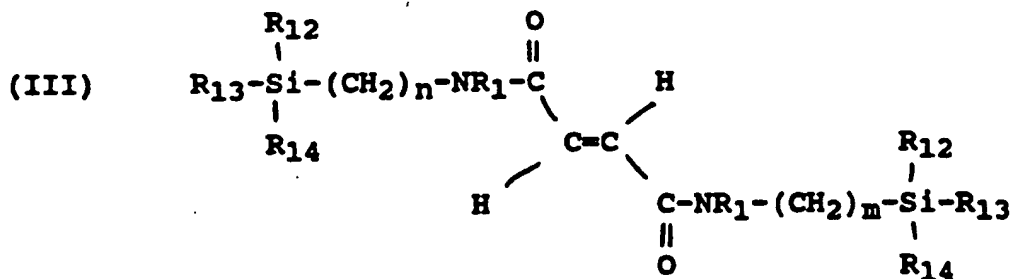
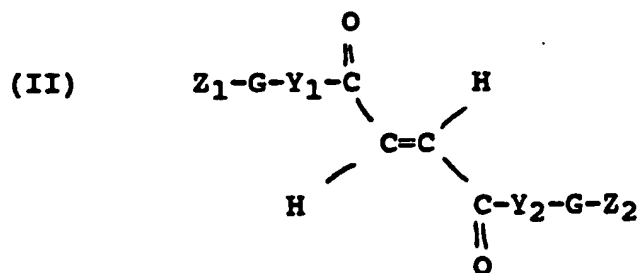
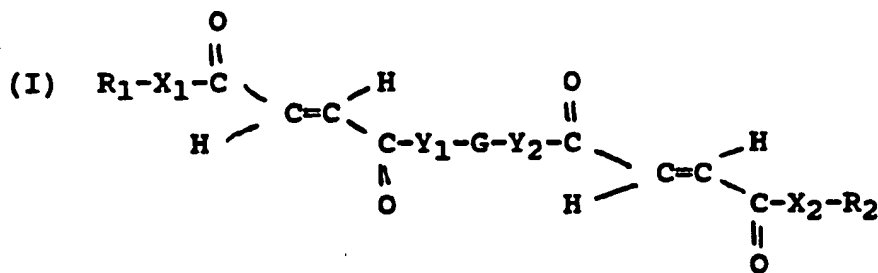
12. The monomer mix of Claim 2 wherein said mix may be cured using a combination of thermal and UV energy.

13. The monomer mix of Claim 2 wherein said mix may be cured using UV energy.

14. A hydrogel made from the monomer mix of Claim 2.

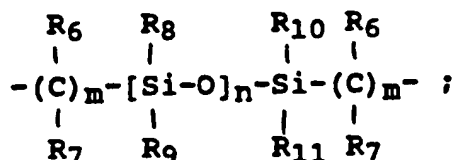
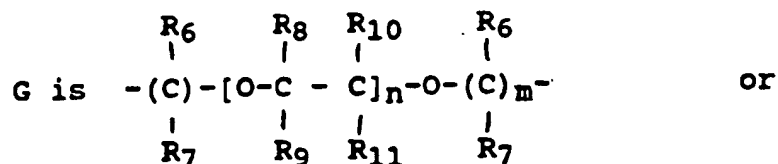
15. A polymerization product produced from a monomer mix comprising:

a) at least one fumarate-containing or fumaramide-containing monomer having the following schematic representations:



wherein





$X_1$ ,  $X_2$ ,  $Y_1$  and  $Y_2$  are independently O or  $NR_4$ , except that when G is siloxane-containing,  $X_1$  and  $X_2$  must be  $NR_4$ ;

$Z_1$  and  $Z_2$  are independently  $OR_3$  or  $NR_4R_5$ ;

$R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$  and  $R_5$  are independently H or an alkyl group having 1 to 10 carbon atoms;

$R_6$ ,  $R_7$ ,  $R_8$ ,  $R_9$ ,  $R_{10}$  and  $R_{11}$  are independently an alkyl-containing group having 1 to 10 carbon atoms, or fluoroalkyl-containing group having 1 to 10 carbon atoms;

$R_{12}$ ,  $R_{13}$  and  $R_{14}$  are independently methyl, trimethylsiloxy or pentylmethyldisiloxanyloxy;

m is 1 to 10;

n is 5 to 100; and

b) at least one hydrophilic monomer.

16. The polymerization product of Claim 15 wherein said hydrophilic monomer is selected from the group consisting of N-vinyl pyrrolidone, N-vinyl-N-methyl acetamide, N-vinyl-N-

ethyl acetamide, N-vinyl-N-ethyl formamide, N-vinyl formamide, N,N-dimethyl acrylamide, 2-hydroxyethyl methacrylate, glycerol methacrylate, 2-hydroxyethyl methacrylamide, methacrylic acid and acrylic acid.

17. The polymerization product of Claim 15 wherein said hydrophilic monomer is N,N-dimethylacrylamide.

18. The polymerization product of Claim 15 wherein said hydrophilic monomer is N-vinyl pyrrolidone.

19. The polymerization product of Claim 15 wherein said material further comprises a hydrophobic monomer.

20. The polymerization product of Claim 15 wherein said material further comprises a bulky polysiloxanylalkyl monomer.

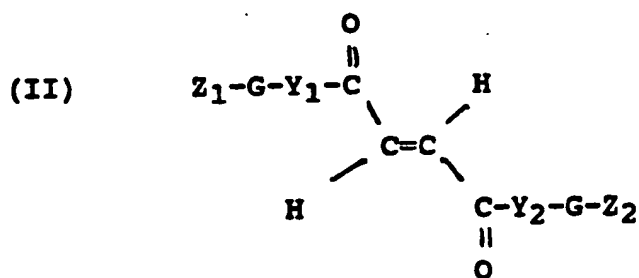
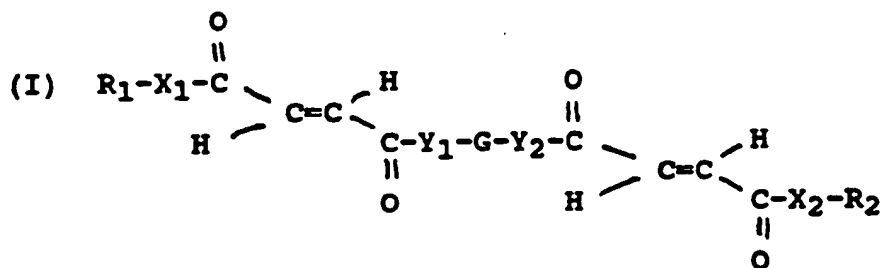
21. The polymerization product of Claim 15 wherein said material further comprises a polyorganosiloxane-containing monomer.

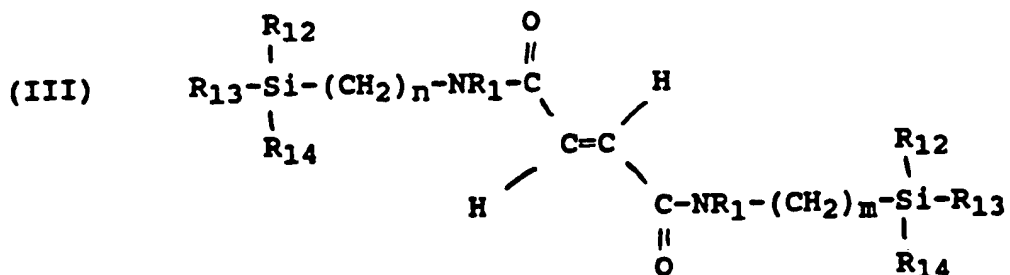
22. The polymerization product of Claim 15 wherein said material is a hydrogel.

23. The polymerization product of Claim 15 wherein said material may be cured using a combination of thermal and UV energy.

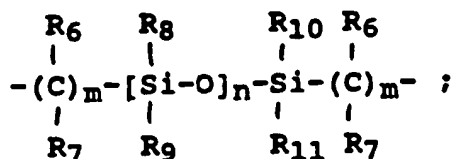
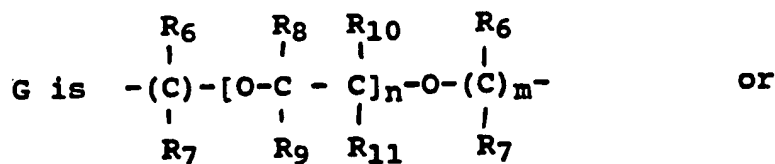
24. The polymerization product of Claim 15 wherein said material may be cured using UV energy.

25. A contact lens produced from a monomer mix comprising  
a) at least one fumarate-containing or fumaramide-containing monomer having the following schematic representations:





wherein



$X_1$ ,  $X_2$ ,  $Y_1$  and  $Y_2$  are independently O or  $NR_4$ , except that when G is siloxane-containing  $X_1$  and  $X_2$  must be  $NR_4$ ;

$Z_1$  and  $Z_2$  are independently  $OR_3$  or  $NR_4R_5$ ;

$R_1, R_2, R_3, R_4$  and  $R_5$  are independently H or an alkyl group having 1 to 10 carbon atoms;

R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub>, R<sub>9</sub>, R<sub>10</sub> and R<sub>11</sub> are independently an alkyl-containing group having 1 to 10 carbon atoms, or fluoroalkyl-containing group having 1 to 10 carbon atoms;

$R_{12}$ ,  $R_{13}$  and  $R_{14}$  are independently methyl, trimethylsiloxy or pentylmethyldisiloxanyloxy;

m is 1 to 10;

n is 5 to 100; and

b) at least one hydrophilic monomer.

26. The contact lens of Claim 25 wherein said hydrophilic monomer is selected from the group consisting of N-vinyl pyrrolidone, N-vinyl-N-methyl acetamide, N-vinyl-N-ethyl acetamide, N-vinyl-N-ethyl formamide, N-vinyl formamide, N,N-dimethyl acrylamide, 2-hydroxyethyl methacrylate, glycerol methacrylate, 2-hydroxyethyl methacrylamide, methacrylic acid and acrylic acid.

27. The contact lens of Claim 25 wherein said hydrophilic monomer is N,N-dimethylacrylamide.

28. The contact lens of Claim 25 wherein said hydrophilic monomer is N-vinyl pyrrolidone.

29. The contact lens product of Claim 25 wherein said material further comprises a hydrophobic monomer.

30. The contact lens of Claim 25 wherein said material further comprises at least one polyorganosiloxane-containing monomer.

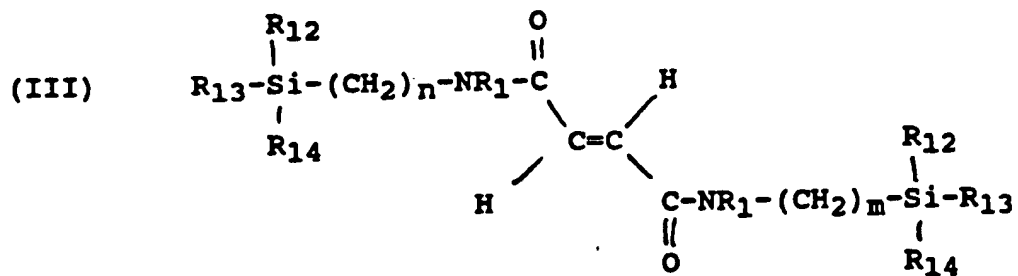
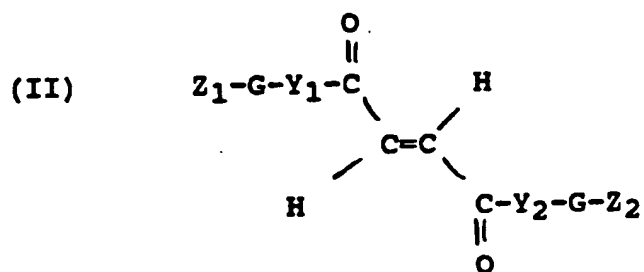
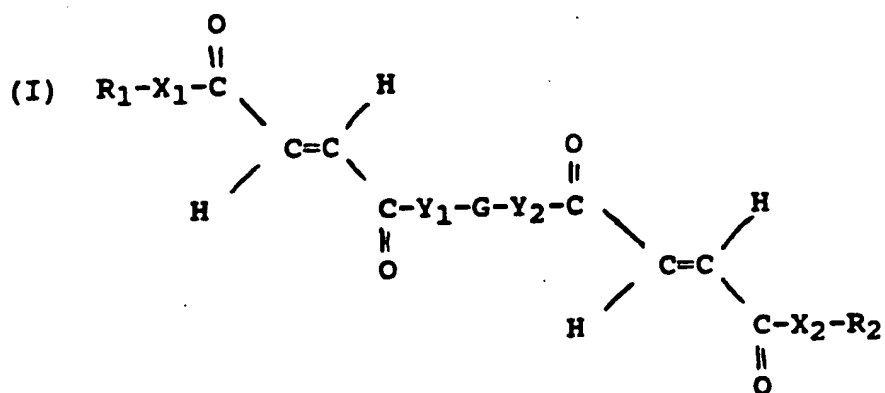
31. The contact lens of Claim 25 wherein said material further comprises a bulky polysiloxanylalkyl monomer.

32. The contact lens of Claim 25 wherein said material is a hydrogel.

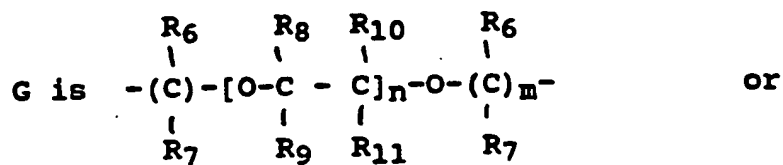
33. The contact lens of Claim 25 wherein said material may be cured using a combination of thermal and UV energy.

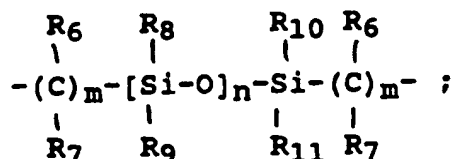
34. The contact lens of Claim 25 wherein said material may be cured using UV energy.

35. A method for preparing a polymerizable material comprising the steps of a) placing into a monomer mix at least one fumarate-containing monomer or fumaramide-containing monomer having the following schematic representations:



**wherein**





$X_1$ ,  $X_2$ ,  $Y_1$  and  $Y_2$  are independently O or  $NR_4$ , except that when G is siloxane-containing  $X_1$  and  $X_2$  must be  $NR_4$ ;

$Z_1$  and  $Z_2$  are independently  $OR_3$  or  $NR_4R_5$ ;

$R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$  and  $R_5$  are independently H or an alkyl group having 1 to 10 C atoms;

$R_6$ ,  $R_7$ ,  $R_8$ ,  $R_9$ ,  $R_{10}$  and  $R_{11}$  are independently an alkyl-containing group having 1 to 10 C atoms, or fluoroalkyl-containing group having 1 to 10 C atoms;

$R_{12}$ ,  $R_{13}$  and  $R_{14}$  are independently methyl, trimethylsiloxy or pentylmethyldisiloxanyloxy;

m is 1 to 10;

n is 5 to 100;

with at least one hydrophilic monomer, and b) curing the monomer mix of step a).

36. The method of Claim 35 wherein said monomer mix further comprises at least one siloxane-containing monomer.



# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/U. 94/02379

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 5 C08F30/08 C08F291/00 C08F22/10 C07C7/08 G02B1/04  
C08F290/06

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 5 C08F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US,A,4 260 725 (P.L.KEOGH) 7 April 1981 ---	
A	EP,A,0 219 884 (TOMEI SANGYO KABUSHIKI KAISHA) 29 April 1987 cited in the application -----	

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents :

- \* "A" document defining the general state of the art which is not considered to be of particular relevance
- \* "E" earlier document but published on or after the international filing date
- \* "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \* "O" document referring to an oral disclosure, use, exhibition or other means
- \* "P" document published prior to the international filing date but later than the priority date claimed

- \* "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \* "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \* "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \* "&" document member of the same patent family

Date of the actual completion of the international search

21 July 1994

Date of mailing of the international search report


- 8. 08. 94

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl,  
Fax (+ 31-70) 340-3016

Authorized officer

Cauwenberg, C



JP-A-	63052518	12-02-88
JP-A-	62099720	09-05-87
JP-C-	1626413	28-11-91
JP-B-	2050450	02-11-90
JP-A-	62106432	16-05-87
DE-D-	3689100	04-11-93
DE-T-	3689100	17-03-94
US-A-	5142009	25-08-92
US-A-	4868260	19-09-89

---